PATENT
4518-0111P

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant:	LOIBNER, Hans et al.	Conf.:
Appl. No.:	NEW	Group:
Filed:	October 7, 2005	Examiner:
For:	IMMUNOGENIC RECOMBINANT ANTIBODY	

L E T T E R

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

October 7, 2005

Sir:

The PTO is requested to use the amended sheets/claims attached hereto *(which correspond to Article 19 amendments or to claims attached to the International Preliminary Examination Report (Article 34))* during prosecution of the above-identified national phase PCT application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment(s)

Claims:

1. Immunogenic recombinant antibody designed for immunization of primates comprising at least a part of a murine IgG2a subtype amino acid sequence and a hamster or primate glycosylation.

2. Antibody according to claim 1 that contains an epitope specific for a tumor associated antigen or fragments thereof.

3. Antibody according to claim 1 that contains a mimotope triggering immune response specific for a tumor associated antigen or fragments thereof.

4. Antibody according to claim 1 or 3 that contains an Ep-CAM mimotope.

5. Antibody according to claim 1 or claim 3 that contains a Lewis-y mimotope.

6. Antibody according to one of the claims 1 to 5, which is a chimeric or humanized antibody.

7. Antibody according to one of the claims 1 to 6, which is an anti-idiotypic antibody.

8. Antibody according to claim 7, which is directed against the idiotype of an antibody specific for a tumor associated antigen.

9. Antibody according to claims 2, 3, 7 or 8, wherein the antigen is selected from the group consisting of peptides or proteins, such as EpCAM, NCAM, CEA and T cell peptides, carbohydrates, such as Lewis Y, Sialyl-Tn, Globo H, and glycolipids, such as GD2, GD3 und GM2.

10. Antibody according to one of the claims 1 to 9, which is a bi-isotopic antibody.

11. Antibody according to one of the claims 1 to 10, wherein the antibody is an IgG1 antibody containing the IgG2a subtype amino acid sequence in the constant region.

12. Antibody according to one of the claims 1 or 11, wherein the IgG2a subtype amino acid sequence is contained in at least one of the regions selected from the CH1, hinge, CH2 and CH3 regions.

13. Antibody according to one of the claims 7 to 12, which is an anti-idiotypic antibody to monoclonal antibodies produced by ATCC HB 9324 or ATCC HB 9347.

14. Vaccine comprising an antibody according to one of claims 1 to 13 in a pharmaceutical formulation.

15. Vaccine according to claim 14, wherein the pharmaceutical formulation contains an adjuvant.

16. Multicistronic antibody expression construct for producing an antibody according to claim 1 in a CHO or HEK293 expression system, which contains at least a nucleotide sequence encoding a kappa light chain and a nucleotide sequence encoding a gamma heavy chain, wherein at least one of the nucleotide sequences encoding a kappa light chain or gamma heavy chain comprises a nucleotide sequence encoding at least a part of a murine IgG2a subtype amino acid sequence, and at least two IRES elements.

17. Antibody expression construct of claim 16, wherein the nucleotide sequence encoding at least the part of the murine IgG2a subtype amino acid sequence is ligated into the nucleotide sequence encoding the kappa light chain or the gamma heavy chain by one of insertion or substitution techniques.

18. Vector comprising a promotor, an antibody-expression construct of one of claims 16 or 17 and a transcription termination sequence.

19. Vector according to claim 18, wherein one of the IRES sequences is attenuated by an inserted sequence that downregulates the entry of the ribosomes.

20. A CHO host cell or a HEK 293 transformed with vector according to claim 18 or 19.

21. A method of producing an antibody according to claim 1 comprising
- transforming a CHO or HEK293 host cell with a multicistronic antibody-expression construct containing at least a nucleotide sequence encoding a kappa light chain and a nucleotide sequence encoding a gamma heavy chain, wherein at least one of the nucleotide sequences comprises a nucleotide sequence encoding at least a part of a murine IgG2a subtype amino acid sequence, and at least two IRES elements, and
-expressing said nucleotide sequences under the control of a single CMV promoter to produce an intact antibody,
-transcription of a single RNA comprising protein sub-units and selection marker.

22. Method according to claim 21, wherein one of the IRES elements is an attenuated IRES sequence, which attenuated IRES sequence downregulates the expression of a quantitative selection marker operably linked thereto.

23. Method according to claim 22, wherein the selection marker sequence is a gene encoding dihydrofolate reductase.

24. Method according to one of claims 21 to 23, wherein the nucleotide sequences are expressed by culturing transfected CHO cells that are deficient in dihydrofolate reductase, preferably in the presence of a selective methotrexate concentration ranging from 1 to 10 µmol/l.

25. Method according to one of claims 21 to 24, wherein the nucleotide sequence encoding the kappa chain and a nucleotide sequence encoding the gamma chain are linked by an IRES sequence.

26. Method according to one of claims 21 to 25, producing the kappa light chain and gamma heavy chain in about equimolar quantity.

27. Method according to one of claims 21 to 26, producing an antibody concentration of at least 1µg/ml, preferably 5-50 µg/ml.

28. Method according to one of claims 21 to 27, wherein the host cell is cultured in a serum free medium.